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Supplementary appendix

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SUPPLEMENTAL MATERIALS

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LIVE-AIR Study Group

Drs. Meghan Lewis, Linda Sher, Michael Bowdish, Noah Wald-Dickler, Subarna Biswas, Lydia Lam, Khang Vo, Roy Poblete, May M. Lee, Douglass Hutcheon from the University of Southern California (USC) Keck and LAC Medical Centers; Drs. Zelalem Temesgen, and Andrew D. Badley, MD from the Mayo Clinic, Rochester MN; Drs. Charles D. Burger and Claudia R. Libertin from Mayo Clinic, Jacksonville FL; Dr. Jason Baker from Hennepin Healthcare Research Institute Minneapolis, MN; Dr. Victoria Catterson from BioSymetrics, Inc., New York, NY; Dr. William S. Aronstein from CTI, Covington, KY; Drs. Cameron Durrant, Dale Chappell, Omar Ahmed, and Gabrielle Chappell from Humanigen, Inc., Burlingame, CA; Drs. Robert Orenstein and Roberto Patron from Mayo Clinic Arizona; Drs. Vincent C. Marconi, Colleen F. Kelley, John Gharbin, Caitlin Moran, Sheetal Kandiah, Valeria Cantos, Paulina Rebolledo, Carlos del Rio, Jeffrey Lennox, Carmen Polito, Paulina Rebolledo, Anandi Sheth from Emory University Medical Center and Grady Memorial Hospital; Drs. Anup Patel, Homero Paniagua from St. Barnabas Medical Center; Dr. Seife Yohannes from MedStar Washington Hospital Center; Drs. Alpesh Amin, Richard Lee, Miki Watanabe, Lanny Hsieh from the University of California-Irvine Medical Center; Drs. Martin Cearras, Amay Parikh, Jason Sniffen, Wilfred Onyia from AdventHealth Orlando; Drs. Christopher Polk, Michael Boger, Lisa Davidson, Kiran Gajurel, Michael Leonard, Lewis McCurdy, Nestor Quezada, Mindy Sampson, Zainab Shahid, Stephanie Strollo, David Weinrib, Sara Zulfigar from Atrium Health; Drs. Cheryl McDonald, John Hollingsworth, John Burk, Joshua Berg, Daniel Barbaro, Andrew Miller, Lakshmi Sambathkumar, Stuart McDonald, Obinna Okoye from Texas Health Harris Methodist Hospital Fort Worth; Drs. Juan Pulido, Jennifer Fulton, William Gill from Baptist Health Research Institute Jacksonville; Drs. Richard Zuckerman, Lionel Lewis from Dartmouth-Hitchcock Medical Center; Dr. Chaitanya Mandapakala from St. Elizabeth Medical Center; Drs. Matthew Robinson, Brian Metzger from St. David's Medical Center; Drs. Maqsood Alam, Chrisoula Politis from Mercy Medical; Drs. Anne Frosch, Linh Ngo from Hennepin Healthcare; Drs. Fernando Carvalho Neuenschwander, Estevão Figueiredo, Gualter Cançado, Gustavo Araujo, Lucas Guimarães from Hospital Vera Cruz (NUPEC) in Brazil; Drs. Ricardo Diaz, Natalia Bacellar, Celso Silva, Paulo Ferreira, from Escola Paulista de Medicina (UNIFESP) in Brazil; Dr. Marina Andrade Lima, Caroline Uber Ghisi, Camila Anton, Ricardo Albaneze from Hospital Dia do Pulmão in Brazil; Dr. Daniel Wagner de Castro Lima Santos, Ana Caroline Iglessias, Marianna Lago, Paula Pietrobom, Maysa Alves from Hospital São Luiz do Jabaquara (IDOR) in Brazil; Drs. Juvencio José Duailibe Furtado, Leopoldo Trevelin, Valeria Telles, Francini Correa from Hospital Heliópolis in Brazil; Drs. Fabiano Ramos, Marina de A. R. Da Silva, Rebeca C. Lacerda Garcia, Ana Elizabeth G. Maldonado, Ana Carolina M. Beheregaray, Ana Maria T. Ortiz from Hospital São Lucas (PUCRS); Drs. Kleber Luz, Eveline Pipolo Milan, Janine Soares de Castro, Matheus José Barbosa Moreira, Renata Bezerra Onofre, Tácito do Nascimento Jácome, Victor Barreto Garcia, Victor Matheus Rolim de Souza from Centro de Pesquisas Clínicas de Natal (CPCLIN) in Brazil; Drs. Felipe Dal Pizzol, Cristiane Ritter, Marcelo B. Vinhas from Sociedade Literaria e Caritativa Santo Agostinho (SLCSA) in Brazil; Drs. Adilson Joaquim Westheimer Cavalcante, Julia Minghini, Loni Dorigo, Marina Salgado Miranda from Centro Multidisciplinar de Estudos Clínicos (CEMEC) in Brazil; Drs. Martti Anton Antila, Rebeca Brugnoli, Henrikki Antila from Consultoria Médica e Pesquisa Clínica (CMPC) in Brazil.

Table S1. Baseline Characteristics in Remdesivir Treated Patients

	Lenzilumab (n=170)	Placebo (n=177)	Total (n=347)
Gender			
Male (%)	114 (67)	113 (64)	227 (65)
Age			
Mean (SD)	62 (14)	63 (14)	62 (14)
Median (min-max)	62 (28-98)	63 (22-96)	63 (22-98)
<65 (%)	104 (61)	103 (58)	207 (60)
≥ 65 (%)	66 (39)	74 (42)	140 (41)
>80 (%)	14 (8)	9 (5)	23 (7)
BMI			
Mean (SD)	34 (9)	32 (7)	33 (8)
≥30 Kg/m ² (%)	103 (60.6)	95 (53.7)	198 (57.1)
Race (%)			
American Indian	3 (2)	0	3 (1)
Asian	10 (6)	5 (3)	15 (4)
Black	31 (18)	28 (16)	59 (17)
White	117 (69)	124 (70)	241 (70)
Multiple	0	0	0
Other	9 (5)	19 (11)	28 (8)
Ethnicity (%)			
Hispanic or Latino	34 (20)	50 (28)	84 (24)
Not Hispanic or Latino	134 (79)	124 (70)	258 (74)
Not Reported	2 (1)	4 (2)	6 (2)
Region (%)			
US	170 (100)	177 (100)	347 (100)
Brazil	0	0	0
Supplemental Oxygen			
Room Air (clinical ordinal score=5)	15 (9)	14 (8)	29 (8)
Low-Flow Oxygen (clinical ordinal score=4)	73 (43)	71 (44)	154 (44)
High Flow Oxygen or NPPV (clinical ordinal score=3)	82 (48)	85 (48)	167 (48)
CRP (mg/L)			
Mean (SD)	101 (77)	96 (72)	98 (74)
Median	81	82	81
IQR	(47-139)	(47-122)	(43-136)
Co-Morbidity (%)			
<i>Cardiovascular</i>			
Hypertension	107 (63)	129 (73)	236 (68)
Congestive Heart Failure	26 (15)	19 (11)	45 (13)
Coronary Artery Disease	27 (16)	27 (15)	54 (15)
<i>Diabetes</i>	97 (57)	110 (62)	207 (59)
<i>Chronic Liver Disease</i>	14 (8)	12 (7)	26 (6)
<i>Chronic Kidney Disease</i>	31 (18)–	28 (16)	59 (17)
<i>Respiratory</i>			
Asthma	24 (14)	16 (9)	40 (12)
Interstitial Pulmonary Fibrosis	3 (2)	0	3 (1)
COPD	17 (10)	16 (9)	33 (10)

Table S2. Primary and Key Secondary Endpoints in Patients Treated Lenzilumab and Concomitant Medications^a

<i>Primary Endpoint – Survival Without Ventilation^b</i>				
Population	Kaplan-Meier Estimate of SWOV Lenzilumab^c (95%CI)	Placebo^c (95%CI)	Lenzilumab v Placebo Hazard Ratio^d (95%CI)	P Value
<i>Remdesivir</i> (n=347)	149 (84%) (78% - 89%) (n=170)	131 (74%) (67% - 80%) (n=177)	1.91 (1.19-3.05)	0.0073
<i>Steroids</i> (n=449)	183 (83%) (78% - 88%) (n=221)	176 (77%) (70% - 82%) (n=228)	1.54 (1.02-2.32)	0.040
<i>Remdesivir and steroids</i> (n=331)	137 (84%) (77% - 89%) (n=163)	123 (73%) (66% - 79%) (n=168)	1.92 (1.20-3.07)	0.0067
<i>Key Secondary Endpoints</i>				
Outcome	Kaplan-Meier Estimates or Estimated Marginal Mean Lenzilumab	Placebo	Hazard Ratio or Odds Ratio (95%CI)	P Value
<i>Incidence IMV, ECMO or death</i>				
<i>Remdesivir</i> (n=347)	26 (13%) (9% - 19%) (n=170)	45 (23%) (17% - 30%) (n=177)	0.51 ^e (0.29-0.89)	0.020
<i>Remdesivir and steroids</i> (n=331)	26 (14%) (9% - 20%) (n=163)	45 (27%) (18% - 32%) (n=168)	0.51 ^e (0.28-0.89)	0.018
<i>Ventilator-Free Days^{g,h} (mean days, SD)</i>				
<i>Remdesivir</i> (n=347)	24 ^f (9) (n=170)	22 ^f (11) (n=177)		0.019 ^f
<i>Remdesivir and steroids</i> (n=331)	24 ^f (9) (n=163)	21 ^f (11) (n=168)		0.018 ^f
<i>ICU Days^h (mean days)</i>				
<i>Remdesivir</i> (n=347)	6 ^f (10) (n=170)	7 ^f (11) (n=177)		0.26 ^f
<i>Remdesivir and steroids</i> (n=331)	6 ^f (10) (n=163)	8 ^f (12) (n=168)		0.23 ^f
<i>IMV</i>				
<i>Remdesivir</i> (n=347)	19 (11%) (7% - 17%)	42 (24%) (18% - 31%)	0.39 ^d (0.23-0.67)	0.0007

	(n=170)	(n=177)		
<i>Remdesivir and steroids</i> (n=331)	20 (12%) (7% - 18%) (n=163)	42 (25%) (19% - 33%) (n=168)	0.39 ^d (0.23-0.67)	0.0007
<hr/>				
<i>Mortality</i>				
<i>Remdesivir</i> (n=347)	18 (11%) (7%-17%) (n=170)	30 (17%) (12%-24%) (n=177)	0.64 ^d (0.36-1.15)	0.13
<i>Remdesivir and steroids</i> (n=331)	18 (11%) (7%-17%) (n=163)	30 (18%) (13%-25%) (n=168)	0.64 ^d (0.35-1.14)	0.13
<hr/>				
<i>Time to Recovery (days)</i>	Quartile	Lenzilumab (95%CI)	Placebo (95%CI)	
<i>Remdesivir</i> (n=347)	25% 50% ^g 75%	5 (5-6) 9 (7-10) 16 (12-22) (n=170)	5 (5-6) 8 (7-9) 25 (14-NA) (n=177)	0.61
<i>Remdesivir and steroids</i> (n=331)	25% 50% ^g 75%	5 (5-6) 9 (7-10) 17 (12-23) (n=163)	5 (5-6) 8 (7-9) NA (17-NA) (n=168)	0.42

^a All data censored at 28 days following enrollment. mITT analysis population

^b Primary endpoint

^c Kaplan-Meier estimates for proportion of patients.

^d Cox Proportional Hazard Model for time to event with age (≤ 65 , > 65) and severity (severe, critical) strata as covariates

^e Odds Ratio with age (≤ 65 , > 65) and severity (severe, critical) strata as covariates

^f mean (SD), Stratified Wilcoxon p value with age (≤ 65 , > 65) and severity (severe, critical) strata as covariates

^g Median, 95%CI

Supplementary Sensitivity Analyses for SWOV

Baseline factors were evaluated for their influence on the primary analysis of SWOV. A univariate analysis demonstrated that the lenzilumab treated effect was consistent across various baseline characteristics with the exception of no remdesivir treatment and patients treated in Brazil although neither observation was statistically significant (Figure S1). Patients with baseline plasma CRP values below the median level of 79 mg/L experienced a statistically greater likelihood of achieving SWOV, relative to placebo (HR, 2·71; 95%CI, 1·23-6·00; nominal p=0·014; Figure S1).

Table S3. Covariate Sensitivity Analyses of Primary Endpoint in mITT Population^a

<i>Primary Endpoint – Survival Without Ventilation</i>		
Covariate	Lenzilumab v Placebo Hazard Ratio ^b (95%CI)	p value
Asthma	1·64 (1.07-2.49)	0.022
COPD/IPF	1·58 (1.04-2.41)	0.0031
Asthma/ COPD/IPF	1·62 (1.06-2.47)	0.025
Diabetes Mellitus	1·55 (1.02-2.36)	0.039
Hypertension	1·58 (1.04-2.40)	0.034
Obesity	1·59 (1.04-2.41)	0.031
Baseline CRP (numeric)	1·81 (1.18-2.78)	0.0068

^a All data censored at 28 days following enrollment. mITT analysis population

^b Cox Proportional Hazard Model for time to event with each individual covariate assessed separately

Table S4. Ventilator Days^a

Population	Ventilator Days		Lenzilumab v Placebo Incidence Rate Ratio (95%CI)	p value
	Lenzilumab	Placebo		
<i>Overall</i> (n=479)	3.5 (8.8) ^b (n=236)	5.4 (10.5) (n=243)	0.65 (0.39-1.07)	0.090
<i>Remdesivir</i> (n=347)	3.6 (9.0) (n=170)	6.3 (11.1) (n=177)	0.51 (0.29-0.90)	0.020
<i>Remdesivir and steroids</i> (n=331)	3.7 (9.1) (n=163)	6.7 (11.3) (n=168)	0.50 (0.29-0.89)	0.018

^a Analysis with Zero Inflated Negative Binomial Regression^b Values are mean (SD) from the mITT population

Table S5. Median and Interquartile Ranges for Ventilator Days and Duration of ICU Stay^a

	Quartile	Ventilator Days		ICU Days	
		Lenzilumab	Placebo	Lenzilumab	Placebo
<i>Overall</i> (n=479)	25%	0	0	0	0
	50% ^b	0	0	0	0
	75%	0	0	6	8
<i>Remdesivir</i> (n=347)	25%	0	0	0	0
	50% ^b	0	0	0	0
	75%	0	2	7	11
<i>Remdesivir and steroids</i> (n=331)	25%	0	0	0	0
	50% ^b	0	0	0	0
	75%	0	15	7	16

^a mITT analysis population^b Median

Table S6. Time (days) to Two-Point Improvement in Clinical Ordinal Scale^a

	Quartile	Lenzilumab (95%CI)	Placebo (95%CI)	p value
<i>Overall</i> (n=479)	25%	4 (4-5)	5 (5-5)	
	50% ^b	7 (6-8)	8 (7-9)	
	75%	13 (11-19) (n=236)	18 (13-NA) (n=243)	0.28
<i>Remdesivir</i> (n=347)	25%	5 (4-6)	5 (5-6)	
	50% ^b	8 (7-9)	8 (7-9)	
	75%	15 (11-22) (n=170)	25 (14-NA) (n=177)	0.55
<i>Remdesivir and steroids</i> (n=331)	25%	5 (4-6)	5 (5-6)	
	50% ^b	8 (7-10)	8 (7-9)	
	75%	16 (11-23) (n=163)	NA (15-NA) (n=168)	0.42

^a mITT analysis population^b Median, 95%CI

Figure S1. SWOV at Day 28 According to Baseline Characteristics. Baseline factors were analyzed in the mITT population. Data are presented as the hazard ratio of lenzilumab compared with placebo and the associated 95%CI. Room Air or low flow O₂ represents clinical ordinal score of 4 or 5. High flow O₂ and/or NPPV represent clinical ordinal score of 3.

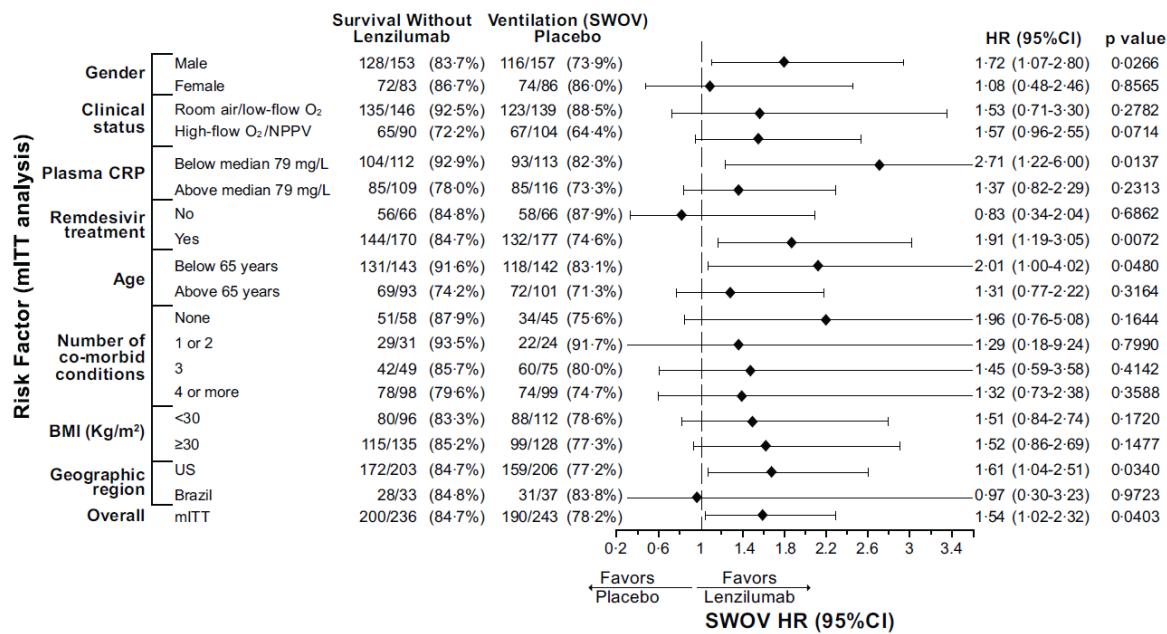
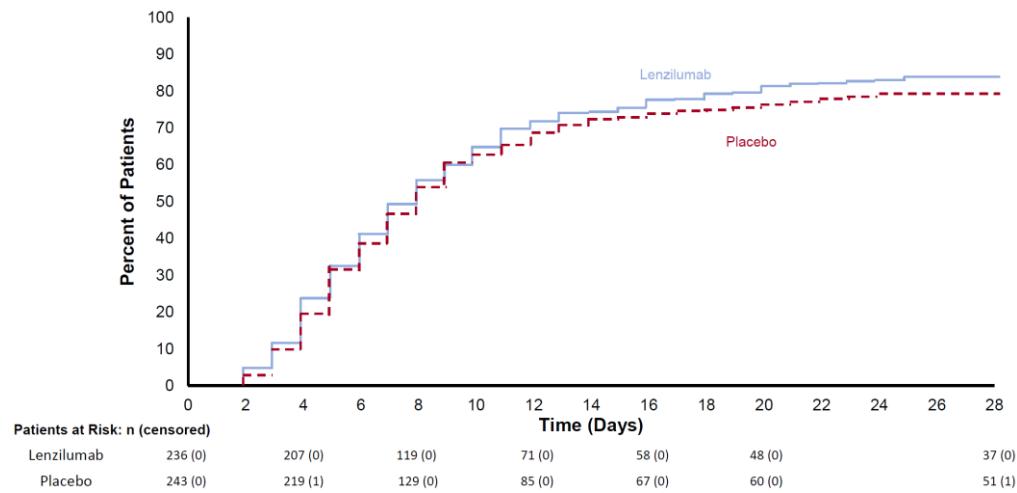


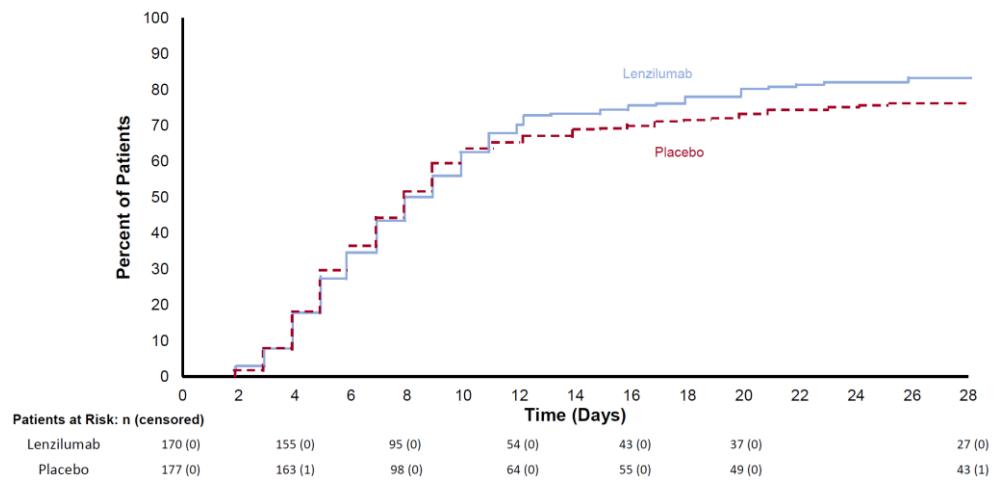
Figure S2. Time to Recovery Following Lenzilumab or Placebo Treatments. Time to recovery, a key secondary endpoint, was defined as the time to achieve ordinal score of 6 (hospitalized, not requiring supplemental oxygen, and no longer requiring ongoing medical care), 7 (not hospitalized, limitation on activities and/or requiring home oxygen), or 8 (not hospitalized, no limitations on activities). **2a.** Time to recovery in the Overall population (lenzilumab, n=236; placebo, n=243). **2b.** Time to recovery in the population treated with remdesivir (lenzilumab, n=170; placebo, n=177). **2c.** Time to recovery in the population treated with remdesivir and corticosteroids (lenzilumab, n=163; placebo, n=168).

Figure S2. Time to Recovery Following Lenzilumab or Placebo Treatments.

S2a



S2b



S2c

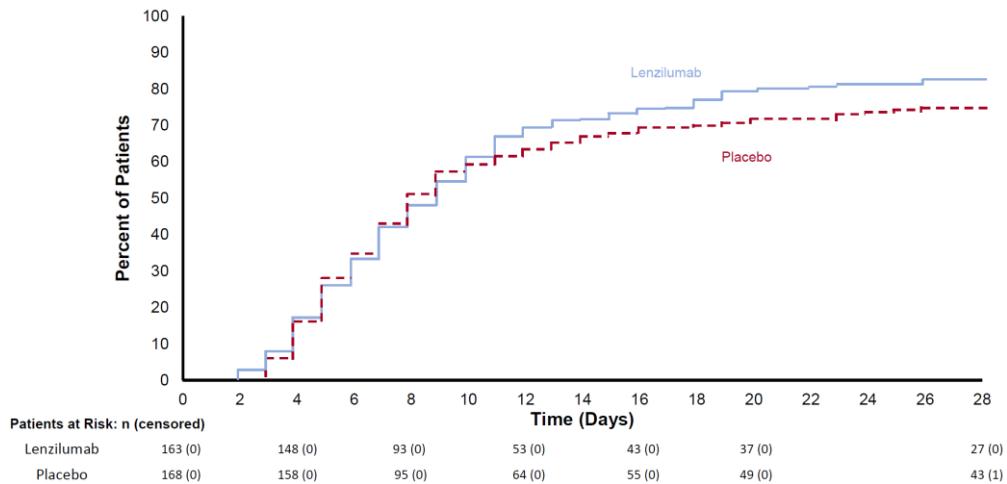
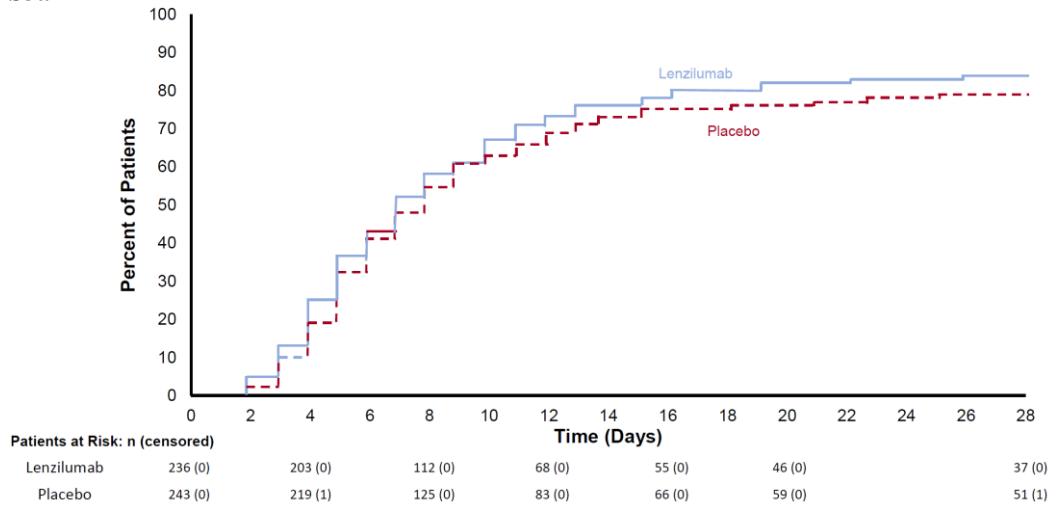


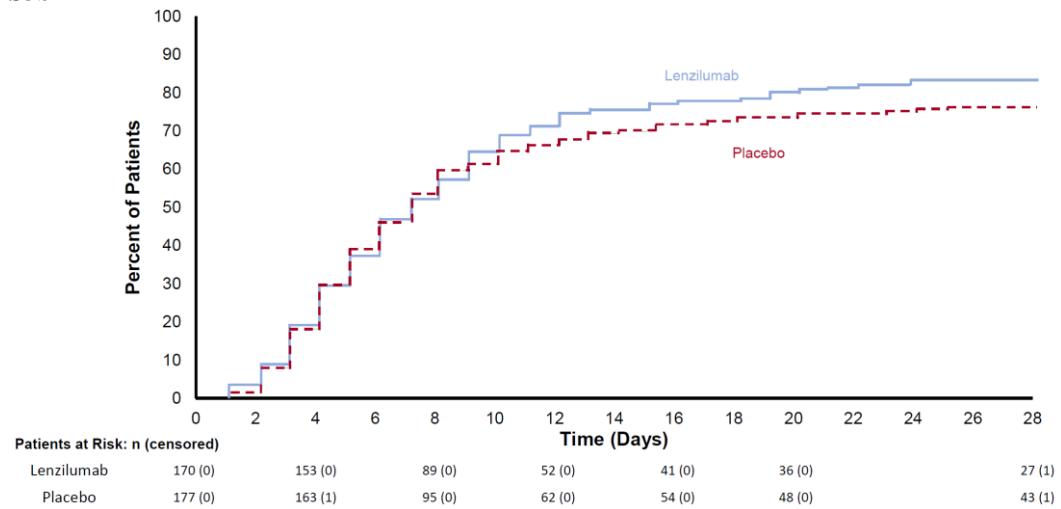
Figure S3. Time to Two-Point Improvement in Clinical Ordinal Scale Following Lenzilumab or Placebo Treatments. **3a.** Time to two-point improvement in the overall population (lenzilumab, n=236; placebo, n=243). **3b.** Time to two-point improvement in the population treated with remdesivir (lenzilumab, n=170; placebo, n=177). **3c.** Time to two-point improvement in the population treated with remdesivir and corticosteroids (lenzilumab, n=163; placebo, n=168).

Figure S3. Time to Two-Point Improvement in Clinical Ordinal Scale Following Lenzilumab or Placebo Treatments

S3a



S3b



S3c

